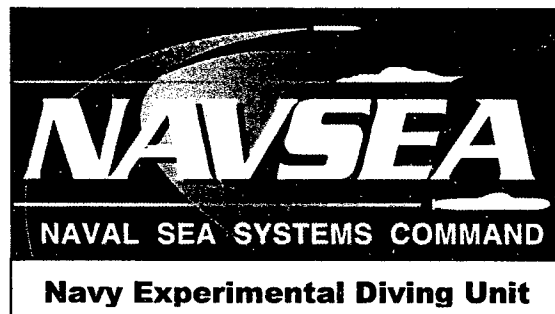


**Navy Experimental Diving Unit
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**PULMONARY EFFECTS OF EIGHT HOURS UNDERWATER
BREATHING 1.35 ATM OXYGEN:
100% OXYGEN OR 16% NITROGEN, 84% OXYGEN**



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INTRODUCTION

The MK 16 MOD 1 underwater breathing apparatus (UBA) maintains the inspired partial pressure of oxygen (P_{O_2}) at 1.3 atmospheres (atm) for depths greater than 33 feet of seawater (fsw). Divers using the UBA breathe gas with variable nitrogen fractions and a constant P_{O_2} . As part of the proposal for the task, "Pulmonary Oxygen Toxicity after Repeated Diving with Elevated Oxygen Partial Pressures,"¹ we had hypothesized that the presence of inert gas in the breathing mixture might protect the lungs from some of the toxic effects of oxygen. We tested that hypothesis by comparing the pulmonary effects of one gas mixture, 16% nitrogen and 84% oxygen, to those of 100% oxygen at the same P_{O_2} .

Preliminary results indicated that the incidence of pulmonary oxygen toxicity after eight-hour dives at $P_{O_2} = 1.35$ atm with 100% oxygen is relatively high: seven of eight divers experienced symptoms, and four had measurable changes in pulmonary function.² The incidence of pulmonary toxic effects with a single four-hour underwater exposure to 100% oxygen at this P_{O_2} is lower: although 16 of 51 divers reported symptoms, only three of them had measurable changes in pulmonary function.³ Because a mechanism that effects discernible improvement after eight hours also probably operates after shorter, more operationally relevant diving exposures, we elected to compare eight-hour dives with 100% oxygen to eight-hour dives with 16% nitrogen, 84% oxygen underwater, both exposures with $P_{O_2} = 1.35$ atm.

We measured pulmonary function and assessed symptoms before diving, immediately after diving, and for several days after those exposures. The pulmonary function variables considered were forced vital capacity (FVC), forced expired volume in one second (FEV_1), peak expired flow or maximum forced expired flow (FEF_{max}), mid forced expiratory flow (FEF_{25-75}), and diffusing capacity of the lung for carbon monoxide (D_LCO). The lower limits of normal for pulmonary function variables were defined as decreases from baseline of 2.4 times the coefficient of variation found for the NEDU population — namely, 7.7% for FVC, 8.4% for FEV_1 , 16.8% for FEF_{max} , 17.0% for FEF_{25-75} , and 14.2% for D_LCO .² We defined decreases of these magnitudes, the lower 95% confidence bands for each variable, as the lower limits of normal.

METHODS

GENERAL

Thirty-one divers breathing mixed gas dove at pressure equivalent to 20 fsw in the Ocean Simulation Facility (OSF) at the Navy Experimental Diving Unit (NEDU), and twenty-three breathing 100% oxygen dove in the NEDU test pool. Divers gave written, informed consent. The dives were controlled and supervised by qualified NEDU personnel. In both sets of dives, subjects used the MK 20 open circuit UBA at rest underwater and breathed humidified gas.

EXPERIMENTAL DESIGN AND ANALYSIS

Before the study, subjects had not been diving while breathing air or mixed gas for one week or while breathing oxygen for two weeks. Except for the experimental dives, they refrained from diving throughout the study period. Each subject's smoking behavior and history of respiratory allergies were noted. General health and use of medications also were recorded during the studies; all were in good health. Ten subjects participated in both dives.

Table 1.
Subject characteristics

Median (range)	100% oxygen			16% N ₂ / 84% O ₂		
Age (Yr)	37	(28–49)		37	(28–49)	
Height (in)	70	(67–75)		70	(66–74)	
Weight (lb)	198	(150–260)		195	(155–260)	
Smoking: (#)	<i>never, former, current</i>			<i>never, former, current</i>		
	16	4	3	22	7	2
Respiratory allergies (#)	2			9		
Medication (#)						
anti-inflammatory	4			9		
anti-allergy	0			3		

The subjects performed pulmonary function tests several days before the test dives, immediately before diving, within 60 minutes of leaving the water, and on working days until the third or fourth day after the test dives. Variables were compared to those from the baseline measurements. If pulmonary function variables on the last of the regular measurement days were below the 95% confidence bands of baseline, pulmonary function was measured again the next day. We used Fisher's Exact Test to assess the incidence of changes in pulmonary function and of symptoms between the two conditions.

Each pulmonary function measurement session involved acquiring three flow volume loops with the tests performed and repeatable according to American Thoracic Society standards.⁴ FVC, FEV₁, FEF_{max}, and other variables were read from the flow volume loops. The sessions also included three single-breath D_LCO measurements made with a 10-second breath-hold. The variables used to obtain D_LCO were calculated from the gas concentrations before and after the breath-hold. Adjustments were made for carboxyhemoglobin and hemoglobin concentrations.⁵ Volumes expired before the gas concentrations were measured, and the volumes of gas over which the concentrations were averaged were chosen to ensure that the analyzer signal was stable when measurements were recorded.⁶

Divers were questioned about specific symptoms (Table 2) while they were underwater and at each pulmonary function measurement session.

Table 2.
Symptoms list

During the dives:	After the dives:
Vision changes	Inspiratory burning
Ringing or roaring in ears	Cough
Nausea	Chest pain or tightness
Tingling or twitching	Shortness of breath
Light-headedness or dizziness	Lowered exercise tolerance
Chest tightness	Unreasonable fatigue
Shortness of breath	Visual complaints
Rapid shallow breathing	Ear problems
Burning on inspiration	
Cough	

EQUIPMENT AND INSTRUMENTATION

The Collins CPL and Collins GS Modular Pulmonary Function Testing System instruments (Ferraris Respiratory; Louisville, CO) were used to measure pulmonary function. The test gas used to measure D_LCO contained 0.3% carbon monoxide and 0.3% methane. A CO oximeter (Instrumentation Laboratory; Lexington, MA) determined the pretest carboxyhemoglobin and hemoglobin concentrations from a venous blood sample.

Divers breathed surface-supplied oxygen from MK 20 open circuit UBAs. The oxygen was humidified by being passed through bubblers built for the purpose. In another series of dives³ we had confirmed that the humidifiers transferred water into the passing gas stream by measuring the water volume before and after some of the dives.

PROCEDURES

In each set of dives, eight subjects dove in a single day. Dive starts were staggered slightly to reduce the wait for pulmonary function measurements after the dives. In the OSF dives, four divers at a time pressed on air to 16 fsw, then donned masks and submerged themselves to recline on a platform about 4 feet underwater. A second group of four locked in to join them 30 minutes later. The first four divers locked out of the chamber after their eight-hour exposure was complete, and the second group exited after the chamber came to the surface at the end of their eight-hour exposure. In the test pool, the diver subjects entered the water at 10-minute intervals.

While underwater, subjects relaxed and watched movies. They were permitted to surface, breathe room or chamber air, and eat or drink for no more than five minutes per

hour. Water temperature was 90 ± 5 °F (32 ± 3 °C). Divers were dressed for comfort: most in swim trunks and T-shirts, but a few in wet suits.

After divers surfaced, they were escorted to the laboratory for blood draws, pulmonary function testing, and recording of symptoms. On the days after diving, the measurements were repeated.

RESULTS

Pulmonary function

Of the 23 subjects who had breathed 100% oxygen, three showed pulmonary function differences from baseline at the first postdive measurement. One subject showed decreases of 10.7% in FVC and 11.0% in FEV₁ without symptoms. The decrements became slightly worse but remained asymptomatic on the following day, with decrements of 11.6% in FVC, 13.4% in FEV₁, and 20.5% in FEF₂₅₋₇₅. All values returned to normal on the second day after diving. Another subject had a decrease of 17.6% in FVC, 21% in FEV₁, and 21% in FEF_{max}, with chest tightness that began after two hours in the water. However, signs and symptoms were completely resolved by the next morning, except for a decrement of 24% in FEF_{max}, a decrement gone two days after diving. The third subject had a decrease of 14.8% in D_LCO, 11.3 % in FVC, and 9% in FEV₁ without symptoms. A mild decrement in FVC persisted for three days after diving.

Of the 31 subjects who had breathed mixed gas, two showed pulmonary function differences from baseline at the first postdive measurement. One subject showed decreases of 9.5% in FVC and 10.2% in FEV₁, accompanied by mild inspiratory burning first reported after six hours in the water. This subject had persistent mild (<10%) decrements in FVC and FEV₁ without symptoms for the two days following his dive. Interestingly, he also participated in the dive with 100% oxygen, with neither sign nor symptom of pulmonary oxygen toxicity. The other subject with an immediate decrease in pulmonary function after mixed gas diving had a decrease of 22.5% in D_LCO accompanied by moderate cough, mild inspiratory burning, and chest tightness. He showed complete resolution of symptoms and recovery of D_LCO to within the lower limits of normal variation for two days after diving, then had an asymptomatic secondary decrease of 19% in D_LCO on the third day after diving before he recovered within the next week. This subject also showed a 23% decrease in D_LCO one day after diving with 100% oxygen.

After having dived while breathing 100% oxygen, four subjects developed pulmonary function changes one or more days later. One subject had a decrease of 23% in D_LCO one day after diving, a decrease accompanied by mild cough, chest tightness, shortness of breath, and exercise intolerance, all of which resolved by the next day. One subject showed deficits of 7.8% in FVC one day after diving and 14.2% in D_LCO two days after diving, with inspiratory burning, cough, and chest tightness first present

one day after diving and lasting two days. Two other subjects first showed changes in pulmonary function two days after diving: one with a 16.4% D_LCO decrease and no symptoms, and one with a 17% FEF_{max} decrease that was preceded by a productive cough one day after diving.

After having dived while breathing mixed gas for eight hours, eight of the 31 subjects developed changes in pulmonary function one or more days later. One subject first showed pulmonary function deficits one day after diving, with decreases of 9.6% in FVC and 12.8% in FEV_1 without symptoms, but with a decrement of 18.6% in FEF_{max} on the third day. Three subjects first showed changed pulmonary function two days after the dive: one with a decrement of 14.7% in D_LCO for one measurement only; one with D_LCO decrements of 16.5% on the second day and of 17.3% on the third day, accompanied on that third day by a 19.5% FEF_{25-75} decrement; and one with a D_LCO decrement of 20.3% followed by a 19.8% FEF_{max} decrement the following day. Five subjects showed first changes in pulmonary function three days after diving: one subject had a deficit of 18.9% in FEF_{25-75} , one of 19.5% in FEF_{max} , one of 14.8% in D_LCO , another of 17.1% in D_LCO , and one had decreases of 9.1% and 10.4% in FVC and FEV_1 , respectively, with those deficits persisting for an additional day at 7.8% and 9.3%, respectively.

The numbers of subjects with any changes in pulmonary function are listed below, by category.

Mixed gas (of 31 subjects): immediate, 2; day one, 1; day two, 3; day three, 10;
and
100% O_2 (of 23 subjects): immediate, 3; day one, 5; day two, 3; day three, 1.

The numbers of divers with any pulmonary function deficit at any time after these dives were 11 of 31 with mixed gas (35%) and 7 of 23 with 100% oxygen (30%); not statistically different. The severity of the changes also was similar for the two dive conditions.

Respiratory symptoms

Of the 31 subjects who had dived for eight hours while breathing mixed gas, 7 reported respiratory symptoms during the dive, 16 on surfacing, and 4 on one of the later days. Of the 23 subjects who had breathed 100% oxygen, 5 reported symptoms during the dive, 10 on surfacing, and 8 on a later day. For both dive conditions, two reports called the symptoms "moderate," and all the others rated them "mild." Thus, either 23% or 22% of the divers reported symptoms during the dives, 52% or 43% on surfacing and 13% or 35% on a later day, for mixed gas or 100% oxygen dives, respectively. Only the proportion of subjects with symptoms on the days after diving differed between conditions; the exact probability of finding 4 of 31 if the true proportion in the population is 8 of 23 is 0.040.

Other effects

Divers commonly experienced Draeger ear (middle ear gas absorption syndrome) and unusual fatigue or exercise intolerance after these dives. Of the divers who breathed mixed gas, 12 (39%) reported ear discomfort and 3 (10%) unusual fatigue or exercise intolerance; of those who breathed 100% oxygen, 9 (39%) reported ear problems and 7 (30%) reported unusual fatigue. Unfortunately, the reports of unusual fatigue depend heavily on an individual's definition of "unusual" in this context.

DISCUSSION

Either absorption atelectasis is not a factor in most pulmonary oxygen toxicity signs and symptoms after eight hours underwater while breathing oxygen at a partial pressure of 1.35 atm, or 16% N₂ is not sufficient to prevent it. Minor absorption atelectasis probably did occur during these dives; immersion during oxygen breathing has been shown to reduce vital capacity significantly after two hours, probably because of atelectasis in dependent alveoli.⁷ Although we have no evidence of large, immediate reductions in vital capacity after oxygen breathing dives, subjects probably engaged spontaneously in reexpansion maneuvers like sighing or yawning, both during air breaks and after they surfaced at the end of the dives. Pulmonary function testing recruits closed areas of the lung, and we averaged three consistent vital capacity values, thus eliminating any measurements when the first value was smaller than the next three.

Although the presence of a nonabsorbable gas in the breathing mixture should help to prevent alveolar collapse, we have evidence that absorption of oxygen had the potential to cause problems in poorly ventilated spaces despite the presence of 16% N₂; the incidence of Draeger ear, an oxygen absorption condition, was the same for both sets of dives.

Published reports suggest that the amount of nonabsorbable gas necessary to prevent atelectasis varies. In one subject who demonstrated airway closure at high lung volume, even 5% N₂ was sufficient.⁸ However, in anesthetized patients, the evidence on the amount of N₂ needed is mixed: in one study, minimal atelectasis (13% of that seen with 100% O₂) was reported when 20% N₂, 80% O₂ was used;⁹ in another using 60% N₂, 40% O₂ after a vital capacity maneuver was shown to prevent postoperative atelectasis.¹⁰ But in a different study, considerable postoperative atelectic reduction in vital capacity was evident in patients who had been given either 30% O₂ or 80% O₂.¹¹

Reexpansion of collapsed alveoli triggers inflammatory cell accumulation.¹² An interesting speculation is that the different reports of unreasonable fatigue may be related to less inflammation after the mixed gas dive than after the dive with 100% O₂. Also, the larger number of delayed symptoms in those who dove with 100% O₂ than in those who dove with mixed gas could be related to prior atelectasis. Since Po₂ was the same for the two sets of dives, the concentration of free radicals generated during the

oxygen exposure should not have differed. More subjects from the mixed gas group were taking anti-inflammatory medication than from the oxygen group — 29% vs. 17% — but more of the mixed gas group also had known respiratory allergies: 29% vs. 9%. Other factors influencing inflammatory processes — for example, subject diet — should have been randomly distributed between the two groups.

CONCLUSIONS

On the whole, the measurable effects of submersion for eight hours while breathing oxygen at a partial pressure of 1.35 atm were not different for 100% O₂ or 16% N₂, 84% O₂. Thus, it is reasonable to use results obtained with 100% O₂ for applications when the same Po₂ is to be obtained at greater depth with N₂ present in the breathing gas. We have not ruled out the possible influence of diffuse atelectasis in later inflammation; deeper dives with larger N₂ fractions than those documented in this study may produce fewer inflammatory changes on later days.

REFERENCES

1. U.S. Naval Sea Systems Command, *Task Assignment 02-22: Pulmonary Oxygen Toxicity after Repeated Diving with Elevated Oxygen Partial Pressures*, 13 Nov 2002, Ser OOC3/3197.
2. B. E. Shykoff, *Pulmonary Effects of Submerged Breathing of Air or Oxygen*, NEDU TR 02-14, Navy Experimental Diving Unit, Nov 2002.
3. B. E. Shykoff, *Repeated Four-hour Dives with $P_{O_2} = 1.35$ atm*, NEDU TR 04-29, Navy Experimental Diving Unit, July 2004.
4. American Thoracic Society, "Standardization of Spirometry 1994 Update," *American Journal of Respiratory and Critical Care Medicine*, Vol. 152 (1995), pp. 1107-1136.
5. *Instruction Manual for the Collins Comprehensive Pulmonary Laboratory* (CPL) (Braintree, MA: Collins Medical, 2000).
6. B. E. Shykoff, *Measurement of Diffusing Capacity for Carbon Monoxide (D_LCO)*, NEDU TR 02-04, Navy Experimental Diving Unit, May 2002.
7. U. I. Balldin, G. O. Dahlback, and C. E. G. Lundgren, "Changes in Vital Capacity Produced by Oxygen Breathing During Immersion with the Head above Water," *Aerospace Med.*, Vol. 42, No. 4 (April 1971), pp. 384-387.
8. T. Turaida, F. T. Nobrega, and T. J. Gallagher, "Absorptional Atelectasis Breathing Oxygen at Simulated Altitude: Prevention Using Inert Gas," *Aerospace Med.*, Vol. 32, No. 2 (February 1967), pp. 189-192.
9. L. Edmark, K. Kostova-Aherdan, M. Enlund, and G. Hedenstierna, "Optimal Oxygen Concentration during Induction of General Anesthesia," *Anesthesiology*, Vol. 98, No. 1 (January 2003), pp. 28-33.
10. Z. Benoit, S. Wicky, J.-F. Fischer, P. Frascarolo, C. Chapuis, D. R. Spahn, and L. Magnusson, "The Effect of Increased F_{IO_2} Before Tracheal Extubation on Postoperative Atelectasis," *Anesthesia & Analgesia*, Vol. 95, No. 6 (December 2002), pp. 1777-1781.
11. O. Akca, A. Podolsky, E. Eisenhuber, O. Panzer, H. Hetz, K. Lampl, F. X. Lackner, K. Wittmann, F. Grabenwoeger, A. Kurz, A.-M. Schultz, C. Negishi, and D. I. Sessler, "Comparable Postoperative Pulmonary Atelectasis in Patients Given 30% or 80% Oxygen during and 2 Hours after Colon Resection," *Anesthesiology*, Vol. 91, No. 4 (October 1999), pp. 991-998.

12. M. Nakamura, S. Fujishima, M. Sawafuji, A. Ishizaka, T. Oguma, K. Soejima, H. Matsubara, S. Tasaka, K. Kikuchi, K. Kobayashi, E. Ikeda, M. Sadick, C. A. Hebert, N. Aikawa, M. Kanazawa, and K. Yamaguchi, "Importance of Interleukin-8 in the Development of Reexpansion Lung Injury in Rabbits," *American J of Respiratory & Critical Care Medicine*, Vol. 161, No. 3, Pt. 1 (March 2000), pp. 1030–1036.